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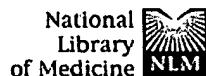
The role of gp130-mediated signals in osteoclast development: regulation of interleukin 11 production by osteoblasts and distribution of its receptor in bone marrow cultures.

Romas E, Udagawa N, Zhou H, Tamura T, Saito M, Taga T, Hilton DJ, Suda T, Ng KW, Martin TJ.

St. Vincent's Institute of Medical Research, University of Melbourne, Victoria, Australia.

Interleukin (IL)-11 is a multifunctional cytokine whose role in osteoclast development has not been fully elucidated. We examined IL-11 production by primary osteoblasts and the effects of rat monoclonal anti-mouse glycoprotein 130 (gp130) antibody on osteoclast formation, using a coculture of mouse osteoblasts and bone marrow cells. IL-1, TNF alpha, PGE2, parathyroid hormone (PTH) and 1 alpha,25-dihydroxyvitamin D3 (1 alpha,25(OH)2D3) similarly induced production of IL-11 by osteoblasts, but IL-6, IL-4, and TGF beta did not. Primary osteoblasts constitutively expressed mRNAs for both IL-11 receptor (IL-11R alpha) and gp130. Osteotropic factors did not modulate IL-11R alpha mRNA at 24 h, but steady-state gp130 mRNA expression in osteoblasts was upregulated by 1 alpha,25(OH)2D3, PTH, or IL-1. In cocultures, the formation of multinucleated osteoclast-like cells (OCLs) in response to IL-11, or IL-6 together with its soluble IL-6 receptor was dose-dependently inhibited by rat monoclonal anti-mouse gp130 antibody. Furthermore, adding anti-gp130 antibody abolished OCL formation induced by IL-1, and partially inhibited OCL formation induced by PGE2, PTH, or 1 alpha,25(OH)2D3. During osteoclast formation in marrow cultures, a sequential relationship existed between the expression of calcitonin receptor mRNA and IL-11R alpha mRNA. Osteoblasts as well as OCLs expressed transcripts for IL-11R alpha, as indicated by RT-PCR analysis and in situ hybridization. These results suggest a central role of gp130-coupled cytokines, especially IL-11, in osteoclast development. Since osteoblasts and mature osteoclasts expressed IL-11R alpha mRNA, both bone-forming and bone-resorbing cells are potential targets of IL-11.

PMID: 8676079 [PubMed - indexed for MEDLINE]



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